IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Sebastian *et al.*
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Confirmation No:	3580
Title:	Utilization of Stem Cell and Fibroblast Combined Products and Nutrients in Topical Compositions

MAIL STOP AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Declaration of Ruslan Semechkin, Ph.D. Under 37 C.F.R. § 1.132

1. I, Ruslan Semechkin, your Declarant, say:

2. I am presently the CEO and President of Lifeline Skin Care, Inc., and Vice President of International Stem Cell Corporation (ISCO). Previously, I served as Senior Research Scientist at ISCO. I received my Ph.D. degree in physiology from Anokhin Research Institute of Normal Physiology, Russian Academy of Medical Sciences, one of the leading Russian biomedical institutes. I am a Member of International Society for Stem Cell Research and a Member of Society of Cosmetic Chemists.

3. At my direction and under my supervision, stem cells from two stem cell cell lines, 2p heterozygous and 12ph homozygous, of human parthenogenic stem cells (hpSCs) were cultivated in hpSC growth medium with and without normal human dermal fibroblast (NHDF) feeder cells. NHDFs were also cultured alone in the same medium. The details of the experiments are recited in Attachment A to this Declaration.

4. As described in Attachment A, equal aliquots of conditioned media collected from separately culturing 2p and 12ph hpSCs on NHDF feeder cells were combined and designated "CM from parthenotes (2p & 12ph) cultivated on fibroblasts". The combined conditioned

medium so obtained was analyzed by ELISA for five growth factors: PDGF, FGF7 (KGF), FGF2 (FGF basic), VEGF, and HGF.

5. Also as described in Attachment A, equal aliquots of conditioned media collected from separately culturing 2p and 12ph hpSCs under feeder-free conditions were combined with a like aliquot of conditioned medium obtained by culturing NHDFs alone. The combined conditioned medium so obtained, designated "CM from parthenotes (2p & 12ph) + CM from fibroblasts", was analyzed by ELISA for five growth factors: PDGF, FGF7 (KGF), FGF2 (FGF basic), VEGF, and HGF.

6. The results of ELISA analyses are presented in Attachment B to this Declaration.

7. The results presented in Attachment B show that the combined conditioned medum obtained by combining medium from culturing hpSCs under feeder free conditions with conditioned media obtained from culturing NHDFs alone ("CM from parthenotes (2p & 12ph) + CM from fibroblasts") has a higher concentration various growth factors compared to conditioned medium obtained from culturing hpSCs in the presence of fibroblast feeder cells ("CM from parthenotes (2p & 12ph) cultivated on fibroblasts").

8. By way of comparison and again with reference to Attachment B, concentrations of FGF2 (bFGF), KGF and HGF are from 18% to 33% higher in "CM from parthenotes (2p & 12ph) + CM from fibroblasts" obtained by combining media from feeder-free culturing hpSCs and separate culturing of NHDFs. The results for PDGF are even more striking. Compared to medium obtained by culturing hpSCs on NHDF feeder cells, the concentration of PDGF is about 85% higher in the mixture of media obtained by combining medium from feeder-free culturing of hpSCs with medium from culturing NHDF cells alone.

9. Further with reference to Attachment B, the concentration of VEGF was almost undetectable in medium conditioned by cultivating hpSCs on NHDF feeder cells. But the amount of VEGF in medium obtained by combining medium from feeder-free culturing of hpSCs with medium from culturing NHDFs alone is considered significant in the art.

10. Mindful of the sanctions for knowing and willful false statements provided for by 18 U.S.C. § 1001 and mindful that knowingly false or misleading statements made herein may adversely affect the validity and enforceability of any patent issuing from the instant application,

I declare that all statements herein based on knowledge are true and that all statements made on information and belief are believed to be true.

11. Further Declarant says not.

Dated: November 4th, 2011

Ruslan Semechkin, Ph.D.

Attachment A to § 1.132 Declaration
of Ruslan Semechkin, Ph.D.

1. Human parthenogenic stem cells (hpSCs) of two different lines, 2p heterozygous and 12ph homozygous, were cultured both with and without normal human dermal fibroblasts (NHDF) feeder cells. NHDFs were also cultured alone.

2. For culturing the hpSCs alone, the 2p and 12ph hpSCs were inoculated onto separate 60mm culture dishes in hpSC growth medium described below.

3. For culturing the hpSCs on NHDF feeder cells, mitomycin C treated NHDFs were seeded on 60mm culture dishes first and, thereafter, inoculated with either 2p hpSCs or 12ph hpSCs in hpSC growth medium.

4. NHDFs were cultured alone in hpSC growth medium in T225 culture flasks.

5. The hpSC growth medium was based on KDMEM/F12 supplemented with 15% KSR, 2 mM L-glutamine, 0.1 mM MEM non-essential amino acids, 0.1 mM ß-mercaptoethanol; 5 ng/ml of bFGF was added just before use.

6. All cells were cultured for 2 days. On the 3rd day after inoculation, the growth medium was replaced with fresh growth medium and incubation (conditioning) continued for 72 hours. After 72 hours, the respective conditioned media were collected, aliquoted into sterile tubes, and stored at -80° C.

7. Equal aliquots of conditioned media from cultivating the 2p and 12ph hpSCs on NHDF feeder cells were combined and designated "CM from parthenotes (2p & 12ph) cultivated on fibroblasts".

8. Equal aliquots of conditioned media from cultivating the 2p and 12ph hpSCs under feeder-free conditions and conditioned medium from culturing NHDF alone were combined and designated "CM from parthenotes (2p & 12ph) + CM from fibroblasts".

9. The combined media described in paragraphs 7 and 8 above were analyzed with ELISA using ELISA kits (Abcam) for five different human growth factors: PDGF, FGF7 (KGF), FGF2 (FGF basic), VEGF, and HGF. All ELISA analysis was performed according to manufacturer's manuals. All the calculations were automatically performed by software for the Biotek Synergy 2 plate reader used.

10. The results are given in the accompanying table and bar chart in Attachment B to this §1.132 Declaration.

Attachment B to § 1.132 Declaration
of Ruslan Semechkin, Ph.D.